

Subject: Minutes of the 2/27/2008 ChemSAC Meeting

To: HED's Chemistry Interest Group

From: HED's Chemistry Science Advisory Council (ChemSAC)

Attendees: Leung Cheng, Christine Olinger, William Donovan (Chair & Minutes), Don Wilbur, Debra Rate, Yvonne Barnes, Bill Cutchin, Rick Loranger, and Tom Bloem.

1. Approve/edit 2/20/08 ChemSAC Meeting Minutes.

The minutes were approved with several editorial clarifications.

2. Genetically modified crops and metabolism studies (T. Bloem). Note: This topic is a follow up to discussion from the previous week.

In a letter dated 21-FEB-2008, Dupont attempted to supply the information requested at last week's ChemSAC meeting: "...the ChemSAC agreed that the registrant will need to provide additional information. They will need to explain, in the absence of data, how the altered ALS [protein] may affect the metabolism pathway and what role it may play."

In addition to the Dupont letter, Rick Loranger supplied the ChemSAC with the following information regarding genetically modified crops from the OECD plant metabolism guidelines:

FROM OECD GUIDELINE "METABOLISM IN CROPS"

"For genetically modified crops that do not involve the insertion of a gene conveying resistance by means of metabolism, no additional metabolism studies are needed. However, the rationale for concluding that the gene does not alter metabolism should be detailed. When a gene is inserted that conveys active ingredient resistance due to pesticide metabolism, then a Metabolism in Crops study should be conducted for each crop grouping (Annex 1) to which the genetically modified crops belong. If one such study shows a similar metabolism to conventional crops, however, no additional studies would be needed. If a different metabolic route is observed, then two additional studies should be conducted."

ANNEX 1

Crops and Crop Groups for Purposes of Metabolism in Crops Studies

Metabolism in crops studies are needed for relevant crops; therefore, for each crop on which use is proposed, a metabolism study is needed from that category. A maximum of three categories is adequate, provided a consistent metabolism picture is obtained from the three studies. Additional categories may need to be studied if there are differences in metabolism across groups.

Code	Category	Crops
F	Fruit	Citrus fruit Tree nuts Pome fruit Stone fruit Berries Small fruit Grapes Fruiting vegetables Banana Persimmon
R	Root crops	Root and tuber vegetables Bulb vegetables
L	Leafy crops	Brassica vegetables Leaf vegetables Stem vegetables Hops Tobacco
C/G	Cereal/Grass crops	Cereals Grass and forage crops
P/O	Pulses and oilseeds	Legume vegetables Pulses Oilseeds Peanuts Legume fodder crops Cacao beans Coffee beans
-	Miscellaneous	In general, crops not listed above or not covered by a grouping are considered as miscellaneous and will not normally be accepted as one of the three crop groups. However, if it is proposed to use such a crop to cover one of the three crop groups due to its national/regional importance, applicants are strongly urged to consult with regulatory authorities.

Information from DuPont indicated that the Optimum™ GAT™ soybean was engineered to express the microbial glyphosate acetyltransferase gene (*gat4601*), which confers tolerance to glyphosate via acetylation of the secondary amine group of glyphosate, and the *gm-hra* gene, which confers tolerance to acetolactate synthase (ALS) inhibiting herbicides by coding for a modified ALS protein. However the Optimum™ GAT™ soybeans produce both a native ALS that is sensitive to ALS inhibitors and the introduced *gm-hra* enzyme that is insensitive to ALS inhibitors. The production of the insensitive *gm-hra* enzyme allows the plant to synthesize essential amino acids and grow normally. With this mechanism of resistance, there is no alteration or metabolism of ALS herbicides by either the native or transgenic enzymes. Therefore, there will be no change in the nature or magnitude of herbicide residue on the Optimum™ GAT™ soybean as compared to conventional soybean.

The ChemSAC agreed that the OECD guidelines are reasonable and should be followed. In the case of ALS resistance in Optimum™ GAT™ soybeans, it appears that the *gm-hra* gene does not change the plant metabolism with respect to the herbicide and thus separate metabolism studies are not needed for crops with this modification. However, in the case of glyphosate resistance in genetically modified crops, the *gat4601* gene confers resistance through modified herbicide metabolism and thus metabolism studies on dissimilar crops containing this gene are appropriate. As additional metabolism studies have already been conducted on Optimum™ GAT™ soybean and corn, the SAC agreed that an Optimum™ GAT™ cotton metabolism study could be waived if the metabolic profile in the Optimum™ GAT™ corn and soybean studies is similar. If not, then an Optimum™ GAT™ cotton metabolism study should be conducted to support this proposed new use.